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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/436,513	11/09/1999	JOHN BRYAN JONES	3290.007US1	6754

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EXAMINER	
PATTERSON, CHARLES L JR	

ART UNIT	PAPER NUMBER
1652	29

DATE MAILED: 04/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/436,513	JONES ET AL.	
	Examin r	Art Unit	
	Charles L. Patterson, Jr.	1652	

-- The MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-11,13,21-57,59,61 and 62* is/are pending in the application.

4a) Of the above claim(s) *21-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,13,51-57,59,61 and 62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 July 2001 and 12 March 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/2/03 has been entered.

Claims 21-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

Claims 1-11, 13, 51-57, 59 and 61-62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *Bacillus lentus* subtilisin N62C-a, N62C-d, N62C-e, N62C-f (R isomer only), N62C-h, N62C-i (R isomer only), S166C-d (S isomer only), S166C-h (S isomer only), S166C-I (S isomer only), L217C-a, L217C-b, L217C-d, L217C-e, L217C-f and L217C-i, does not reasonably provide enablement for the scope of the instant claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. This rejection is repeated for the reasons given in the last two actions and in the advisory. Applicants arguments have been carefully considered but do not overcome the instant rejection.

Applicants urge that the instant claims "were rejected under 35 USC 112, first paragraph, because, according to the Advisory Action, contrary to the assertion in the Office Action, the specification does not indicate why

the Amidase/Esterase ratio is important...[and that the] Examiner has not communicated why 'important' is at issue (see, e.g. Examiner, see e.g. MPEP 2164.03, 2163.04, etc.) in spite of the fact that Applicants have satisfied this request (see Response dated December 3, 2002)...[and that a]ccordingly, reconsideration and withdrawal of the rejection are respectively requested". Some of these statements are not understood by the examiner. Is the "Office Action" referred to *supra* meant perhaps to indicate applicants' reply? An "office action" is a communication sent out by the office to applicants, not a reply sent by applicants to the office. How is the advisory action contrary to the office action? The examiner has looked at MPEP 2164.03 and this section deals with predictability with regard to enablement. MPEP 2163.04 deals with written description, which is not at issue here. Neither section appears to be probative on the instant rejection.

In the instant case, as stated previously, the scope rejection is not based on whether the specification is enabled as to how to make the claimed invention but rather on whether the specification is enabled as to how to use the invention. Does the mutant strain have some useful property that the unmutated strain does not. As discussed in the advisory action, applicants previous submission mistakenly referred to page 18, lines 19-20, when what was apparently meant was page 19, lines 4-5 of the substitute specification, which is now the pending specification. These lines state that the "chemically modified mutants are typically screened for the activity or activities of interest...[such as] the ratio of amidase to esterase activity". However, in reviewing the reply filed 4/15/02, applicants refer to page 21, lines 14-20, which does give an explanation as to the importance of the esterase/amidase ratio. A table is also given in that reply (page 7) that is stated to show "enzymes...having lower than wild-type amidase or esterase activity, and a

better than wild-type amidase/esterase ratios". It is presumed that these mutant value were derived from Table 1, however the "enzyme" is listed as e.g. "S166-**a**(S)" when Table 1 lists the enzyme as "S166C-**a**(S)". If applicants will clarify whether the numbers in this table come from the values in Table 1 of the specification and whether e.g. "S166-**a**(S)" is meant to be "S166C-**a**(S)", then the examiner might modify the instant rejection. It is noted that N62C-e has the most change in the esterase activity from the wild-type.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-11, 13, 51-57, 59 and 61-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berglund, et al.(A or C2). This rejection is repeated for the reasons given in the last two actions. Applicants arguments have been carefully considered but do not overcome the instant rejection.

Applicants state that the advisory action "seems to state (or imply, though it certainly is not clear) that Applicants recited claim language, 'chiral', is within the broad proposition, '...the opportunities for generating catalysts with other improved properties, such as changed specificities, are self-evident...' provided in the art, without giving any (facial) textual support for that bald assertion". Applicants urge "that the art must teach or suggest the claimed limitation, and the burden of communicating the basis

for the rejection is on the Examiner". Applicants original claims were drawn to a modified serine hydrolase that had the thiol hydrogen replaced with one of 5 different substituents. In reply to the first action, applicants limited to enzyme only to those having a chiral substituent. The instant reference teaches all of the embodiments of the instant claims except for specifically mentioning "chiral". However, as stated *supra*, the specification does state that they have the opportunity "for generating catalysts with other improved properties, such as changed specificities and stabilities, are self-evident and are being explored". Therefore the instant reference envisions using other substituents and one well known substituent is a chiral compound. Even if the reference did not specifically mention that other catalysts are self-evident, it would have been obvious to make them. Since it was known that some substituents are chiral and some are non-chiral, either or both could be used in the process taught by the instant reference.

The argument here is similar to arguing that it would not have been obvious to use blue reagents because blue reagents were not specifically mentioned in the reference but blue reagents were known to exist among other types such as red, green, charged, uncharged, etc. It is maintained here that claims drawn generically to a serine hydrolase modified with a thiol reagent having a chiral side chain would have been obvious over the cited prior art. It is maintained that particular mutant stains, such as N62C-e, may be allowable if they have unexpected results, but the generic method is obvious over the cited references.

It would have been obvious to one of ordinary skill in the art to modify serine hydrolases according to the instant reference and assay them for activity, absent unexpected results. The motivation would have been to use the method as a means of mutating serine hydrolases to obtain different

mutant enzymes that may have some useful property.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose telephone number is 703-308-1834. The examiner can normally be reached on Monday - Friday, 7:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone number is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Charles L. Patterson, Jr.
Primary Examiner
Art Unit 1652

Patterson
April 24, 2003